UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,883	12/05/2001	Kenneth W. Dobie	RTS-0337	2873

35807 7590 09/22/2004

FENWICK & WEST LLP
801 CALIFORNIA STREET
MOUNTAIN VIEW, CA 94014

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,883	DOBIE ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-14,19 and 20* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-5-01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 7-6-04.

Claims 1-20 are pending in the instant application.

Election/Restrictions

Claims 15-18, and the sequences listed in claim 3 other than SEQ ID NO: 23, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7-6-04.

Applicant's election without traverse of Group I, claims 1-14, 19, 20, and SEQ ID NO: 23 in the reply filed on 7-6-04 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-14, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to antisense oligonucleotides that specifically target and inhibit the expression of a nucleic acid molecule encoding NOD1, or antisense oligonucleotides that specifically target and differentially inhibit the expression of a variant of NOD1, relative to the remaining variants of NOD1. The specification and claims do not adequately describe elements that are essential to the broad genera comprising nucleic acids encoding NOD1, or variants thereof, nor do they adequately describe antisense that target one of the variants and differentially inhibit it, compared to the remaining variants to NOD1. The scope includes numerous structural variants and the genus is highly variant because it encompasses a large array of molecules. The specification teaches the nucleotide sequence of human NOD1, encoded by SEQ ID NO: 3, portions of the intron/exon junctions of human NOD1 (see Table 1, pages 82-85), and nucleotide sequences encoding a subset of previously identified human NOD1 variants (see Table 2, pages 85-89). But these sequences represent only a subset of the broad genus comprising nucleic acids encoding NOD1, which encompasses NOD1 from any species, and variants of NOD1, human or otherwise. Numerous variants of NOD1 exist in humans alone, and these variants of NOD1 are currently under investigation in various laboratories around the world (see for example Zouali et al, Gut, 52: 71-74, at the abstract on p. 71, Table 2 and last full paragraph on p. 72, describing mutations found in NOD1 in a limited human population sampling). Concise structural features distinguishing structures within the genera (e.g. nucleotide sequences encoding any NOD1, from any species, and variants that are differentially inhibited by an antisense oligonucleotide compared to the remaining variants) from others is missing

from the claims and the disclosure. The specification fails to teach or adequately describe a representative number of species of the genera comprising nucleic acids encoding NOD1, and variants of NOD1, and further whereby an antisense oligonucleotide would differentially inhibit the expression of one of the myriad of variants over the remaining variants. Because the genera are so highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genera claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 2, 4-6, 8-14, 19 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Bertin.

Bertin (USPN 6,469,140) teach compositions comprising a pharmaceutically compatible diluent (e.g. water), a colloidal dispersion system (see col. 37, line 17-col. 38, line 45) and antisense oligonucleotides that target at least an 8 nucleobase portion of an active site on a nucleic acid molecule encoding NOD1, and specifically inhibit its expression in vitro (col.4, lines 15-26; col. 10, lines 31-45; col. 19), or specifically target a splice variant of NOD1, including human and murine CARD4-L, human CARD4-S and CARD4-Y (col. 2, line 41-col. 4, line 14; cols. 9-11; col. 19), and which antisense oligonucleotide further comprises a phosphorothioate internucleotide linkage, a 5-methyl cytosine modified nucleobase, a 2'-O modified sugar residue, and may optionally comprise a chimeric oligonucleotide (see col. 20, line 1-col. 22, line 34).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-14, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bertin as applied to claims 1, 2, 4-6, 8-14, 19 and 20 above, and further in view of McKay et al.

The claims are drawn to a composition comprising an antisense oligonucleotide between 8-50 nucleobases in length that specifically hybridizes to at least an 8 nucleobase portion of an active site on, and inhibits the expression of, NOD-1, which composition further comprises a pharmaceutically acceptable diluent (e.g. water) and a colloidal dispersion system, and which antisense oligonucleotide further comprises a phosphorothioate internucleotide modification, a 2'-O-methoxyethyl modified sugar moiety, and a 5'-methylcytosine modified nucleobase, and which antisense is optionally chimeric.

Bertin is relied upon as cited in the 102 rejection above.

The primary reference of Bertin does not teach the incorporation of 2'-O-methoxyethyl sugar moieties into antisense.

McKay et al (USPN 6,133,246, filed 4-7-1999) teach the incorporation of 2'-O-methoxyethyl sugar moieties into antisense (see col. 8, lines 39-50).

It would have been obvious to one of ordinary skill in the art to incorporate 2'-O-methoxyethyl sugar modifications into antisense oligonucleotides because these modifications were well known in the art at the time the invention was made and one would have been motivated to incorporate these modifications into antisense oligonucleotides because McKay et al teach 2'-O sugar modifications, including 2'-O-methoxyethyl modifications for increasing oligonucleotide stability, target binding and cellular uptake. One of ordinary skill in the art would have expected that antisense oligonucleotides with this sugar modification taught by McKay would have provide increased stability of the antisense. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

SEQ ID NO: 23 appears free of the prior art searched and of record. Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form (and amended to comprise SEQ ID NO: 23 only, and not the other sequences presently claimed in claim 3) including all of the limitations of the base claim and any intervening claims.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices

published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ
TC 1600

JZ
9-18-04